REMARKS

I. Status of the Claims

Claims 6-11 and 22-35 are pending in this application. Claims 6-11 and 31-35 have been withdrawn as directed to a non-elected invention.

By this amendment, Applicant proposes to amend claim 22 by deleting the word "intact" and by reciting that the hybridizing conditions are "of moderate stringency." Support for reciting that the biological sample comprises cells can be found throughout the specification, including, for example, in Examples 2-7, as discussed in further detail below. Support for conditions of "moderate stringency" can be found in the specification, including, for example, at page 9, last paragraph. The proposed amendment does not introduce new matter.

Applicant respectfully requests that the Examiner enter this Amendment under 37 C.F.R. § 1.116, placing the pending claims in condition for allowance. Applicant submits that the proposed amendments do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. Therefore, this Amendment should allow for immediate action by the Examiner. Furthermore, the proposed amendment would place the claims in better form for appeal, should an appeal be necessary.

II. Oath/Declaration

The Office maintains its objection to oath or declaration as allegedly defective. Office Action at 2. According to the Office, the application presents method claims that do not satisfy the requirements of 35 U.S.C. §§ 101 and 112. Office Action at 3-4. Therefore, the Office asserts that Applicant must submit a new oath or declaration designating this application as a continuation-in-part, rather than a continuation of parent Application No. 09/534,072. For the

reasons of record and the arguments presented below, Applicant submits that the claims satisfy the requirements of 35 U.S.C. §§ 101 and 112. Accordingly, Applicant respectfully requests that the Office withdraw this objection.

III. Priority

The Office continues to deny Applicant's priority claim under 35 U.S.C. §119(e) and/or 102, 121, or 365(c) for benefit of the parent application (Application No. 09/435,072 filed March 24, 2000) and Provisional Application 60/126,469 filed March 26, 1999. Office Action at 9. As with the alleged defect in the declaration, the Office states that the earlier-filed applications fail to provide adequate written description support or enablement for the methods of claims 22-30. *Id.* at 9-10. For the reasons of record and in view of the additional arguments provided below in response to the Office's §§ 101 and 112 rejections, Applicant submits that the priority applications provide support under 35 U.S.C. §112, first paragraph for the subject matter of claims 22-30.

The Office further contends that claims 22-30 do not properly benefit from the earlier filing date of Provisional Application 60/126,469 because "it appears the provisional application describes another different nucleotide sequence, which differs from the nucleotide sequence of SEQ ID NO:1 at position 302." *Id.* at 10. This issue has been addressed in parent Application No. 09/435,072, where Applicant submitted declarations by co-inventor Vasantha Srikantan explaining that the single nucleotide discrepancy at position 302 represented a sequencing error and that there was support in the specification as filed, and in Provisional Application 60/126,469, for changing nucleotide 302 from a thymine to a guanine. In response to the declarations and Applicant's arguments, the Office withdrew a new matter rejection and approved an amendment to Figure 8 whereby nucleotide 302 of SEQ ID NO:1 was changed from

a thymine to a guanine. When the instant application was filed, Applicant amended Figure 8 to make the same change to SEQ ID NO:1 that was made in the parent application. This amended version of Figure 8 has been approved in the instant application without objection. Thus, for the reasons of record in parent Application No. 09/435,072, Applicant submits that the priority applications provide support for the nucleotide sequence of SEQ ID NO:1 as currently set forth in the sequence listing of this application.

IV. Objection to Specification

1. Statement of Continuity

The Office maintains its objection to the specification, asserting that "the statement of continuity improperly indicates that this application is a continuation of prior filed Application No. 09/534,072 [and] should be redesignated as a continuation-in-part." Office Action at 11. As with the allegedly defective oath or declaration, the Office bases this objection on its assertion that the claims do not satisfy the requirements of 35 U.S.C. §§ 101 and 112. For the reasons of record and the arguments presented below, Applicant submits that the claims satisfy the requirements of 35 U.S.C. §§ 101 and 112. Accordingly, Applicant respectfully requests that the Office withdraw this objection.

2. Trademarks

The Office maintains the objection to the use of improperly demarcated trademarks, noting that paragraph [0113] of the published application refers to Amplitaq Gold without the appropriate symbol indicating its proprietary nature. Office Action at 12. The specification has been amended to indicate the appropriate symbol of this trademark. Accordingly, Applicant respectfully requests that the Office withdraw this objection.

3. Antecedent Basis

Citing M.P.E.P. §608.01(o), the Office maintains the objection to claims 22-30 as allegedly failing to provide proper antecedent basis. Office Action at 12. Specifically, the Office asserts that while the disclosure describes detecting a marker of prostate cancer by hybridization with an oligonucleotide probe and describes a method of detecting prostate cancer by detecting PCGEM1 RNA and correlating it with the presence of prostate cancer, "it does not provide properly clear and sufficient antecedent basis for the claimed processes." *Id.* For the reasons of record and the arguments provided below in response to the Office's written description rejection, Applicant submits that the application provides proper antecedent basis and clear support for claims 22-30. Accordingly, Applicant respectfully requests that the Office withdraw this objection.

V. Rejection Under 35 U.S.C. §101

The Office maintains its rejection of claims 22-30 under 35 U.S.C. § 101, alleging that "the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility." Office Action at 13. Specifically, the Office asserts that

> 101 requires that an invention have either an immediately obvious or fully disclosed "real world" utility, which the claimed invention lacks because the specification does not disclose a currently available "real world" use for the claimed method of detecting a PCGEMI nucleic acid in a biological sample.
>
> To employ the disclosure of the claimed method of detecting a PCGEM1 nucleic acid in a biological sample in any useful process would require further research, which should be regarded as constituting part of the inventive process. Because the specification does not disclose a currently available, "real world" use for the claimed invention, the requirements set forth under 35 U.S.C. § 101 have not been met.

Office Action at 16-17. Applicant respectfully traverses this rejection for at least the reason that the specification describes several "real world" uses for the claimed methods of detecting a PCGEM1 nucleic acid in a biological sample.

According to the M.P.E.P., "[i]f the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." M.P.E.P. §2107. "The threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999) (reversing summary judgment of invalidity because invention that served the purpose of making one product look like another product provided a specific sufficient benefit to have utility under § 101). Furthermore, utility does not require that every stated objective of the invention be met. All that is required is that the claimed invention meets at least one stated objective. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958-59, 220 USPQ 592, 598 (Fed. Cir. 1983) ("When a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown.").

1. Detecting a PCGEM1 Nucleic Acid in a Method of Detecting Prostate Cancer

Here the specification discloses several specific and substantial uses for the claimed method, including detecting prostate cancer. Even the Office acknowledges that the claimed methods can be used as an active step in a process for detecting prostate cancer. Office Action at 15 ("Still, because the claimed invention elicits no specific effect, nor has any particular function beyond the detection of a PCGEM1 nucleic acid in a biological sample, it is submitted that the disclosure thereof by the specification, as filed, would not make apparent *how* the invention is to be used in any manner that might be regarded both specific and substantial - if not as a mere active step, which is to be taken during the practice of the process of detecting prostate cancer, which is the subject matter of the non-elected invention.") Furthermore, the Office acknowledges that the disclosed methods of detecting prostate cancer "might now be encompassed by the broader scope of the instant claims, but which is the subject matter of the non-elected invention that have been withdrawn from further prosecution." *Id.* at 14.

Nevertheless, the Office apparently dismisses this asserted utility of detecting prostate cancer—not because such a utility is not specific and substantial—but because methods of detecting prostate cancer have been withdrawn as a non-elected invention. *Id.* at 14 and 18 ("Contrary to Applicant's argument, the claimed invention does not have immediately obvious real world utility of detecting a specific, disease-associated nucleotide target - it is instead the subject matter of a non-elected invention that has such an asserted utility.") In so doing, the Office essentially asserts, without any support, that an asserted utility for a withdrawn species cannot be used to support the utility of a generic claim that covers the species. Not only does the Office fail to support its position with any authority but its position is also directly at odds with the guidance provided by the M.P.E.P. Specifically, the M.P.E.P. states that "[w]here an applicant has established utility for a species that falls within an identified genus of compounds,

and presents a generic claim covering the genus, as a general matter, that claim should be treated as being sufficient under 35 U.S.C. 101." M.P.E.P. § 2107.02.

Here, a method of detecting a PCGEM1 nucleic acid can be used as an active step in a method of detecting prostate cancer, as taught in the specification and acknowledged by the Office. Applicant submits that this is a specific and substantial utility. Furthermore, a method of detecting a PCGEM1 nucleic acid in a biological sample is generic to a method of detecting prostate cancer (by detecting a PCGEM1 nucleic acid in a biological sample). Thus, having established a utility for a species of detecting prostate cancer, the more generic claim of detecting a PCGEM1 nucleic acid should similarly be treated as being sufficient under 35 U.S.C. §101. M.P.E.P. § 2107.02. Accordingly, the claimed invention meets at least one stated utility in the specification and, therefore, satisfies 35 U.S.C. §101. *See Raytheon*, 724 F.2d at 958-59, 220 USPQ at 598.

2. *Detecting a PCGEM1 Nucleic Acid in a Method of Identifying an Androgen-Responsive Cell Line*

Other specific and substantial utilities support the claimed methods of detecting a PCGEM1 nucleic acid in a biological sample. For example, the specification discloses that detecting a PCGEM1 nucleic acid can be used to in a method to identify an androgen-responsive cell line. Specifically, the specification states:

> This invention also provides a method of identifying an androgen-responsive cell line, which comprises (a) obtaining a cell line suspected of being androgen-responsive, (b) incubating the cell line with an androgen; and (c) detecting PCGEM1 mRNA in the cell line, wherein an increase in PCGEM1 mRNA, as compared to an untreated cell line, correlates with the cell line being androgen-responsive.

Specification at page 14, lines 3-7; original claim 16.

3. *Detecting a PCGEM1 Nucleic Acid in a Method of Measuring Responsiveness to Hormone-Ablation Therapy*

The specification also discloses that detecting a PCGEM1 nucleic acid can be used in a method to measure the responsiveness of a prostatic tissue to hormone-ablation therapy. Specifically, the specification states:

> The invention further provides a method of measuring the responsiveness of a prostatic tissue to hormone-ablation therapy, which comprises (a) treating the prostatic tissue with hormone-ablation therapy; and (b) measuring PCGEM1 mRNA in the prostatic tissue following hormone-ablation therapy, wherein a decrease in PCGEM1 mRNA, as compared to an untreated cell line, correlates with the cell line responding to hormone-ablation therapy.

Specification at page 14, lines 8-13; original claim 17.

4. Detecting a PCGEM1 Nucleic Acid as a Marker for Diseases that Map to Region 2q32 of Chromosome 2

As noted in the previous response, PCGEM1 nucleic acids can serve as a marker for specific diseases that map to region 2q32 of chromosome 2. In reply, the Office asserts "which diseases are those, if not prostate cancer?" Office Action at 20. As discussed in the specification, however, Applicant discovered that PCGEM1 maps to a specific location of a specific chromosome, namely region 2q32 of chromosome 2. Accordingly, detecting a PCGEM1 nucleic acid can be used to analyze abnormalities associated with gene mapping to chromosome 2 and in particular to region 2q32, which is known to be associated with specific diseases, including diabetes mellitus and T cell leukemia/lymphoma. Specification at page 17. Thus, detecting a PCGEM1 nucleic acid can be used to identify genetic abnormalities in region 2q32 associated with specific diseases, such as diabetes and T cell lymphoma or leukemia.

As discussed above, the specification discloses several specific and substantial utilities for the claimed invention, providing immediate real-world use. As such, the claims satisfy the requirements of 35 U.S.C. §101. *See Raytheon*, 724 F.2d at 958-59, 220 USPQ at 598 ("When a properly claimed invention meets at least one stated objective, utility under § 101 is clearly

shown."). Accordingly, Applicant respectfully requests that the Office withdraw this rejection.

VI. Rejections Under 35 U.S.C. §112, Second Paragraph

The Office maintains the rejection of claims 22-30 under 35 U.S.C. §112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter the applicant regards as the invention." Office Action at 21. The Office asserts that "[t]o satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, the claims must define the metes and bounds of the subject matter that is regarded as the invention by Applicant with the clarity and particularity necessary to permit the skilled artisan to know or determine infringing subject matter." *Id.* at 22. According to the Office, Applicant has not done this in the instant application because

> the subject matter that is now claimed appears to be but a mere step in the originally disclosed process of detecting prostate cancer, which was perhaps all that Applicant originally intended to disclose, since any other contemplated use for the invention cannot be gleaned from a reading of the disclosure. Therefore, even in light of the disclosure, it is submitted the claims fail to clearly and particularly delineate the metes and bounds of the subject matter that is actually regarded as the invention, so as to permit the skilled artisan to know or readily determine infringing subject matter.

Id. at 21-22. Applicant respectfully traverses this rejection.

The Office bases this §112, second paragraph rejection on its finding that the only asserted utility in the specification for the claimed methods is for detecting prostate cancer, subject matter that has been withdrawn from consideration as directed to a non-elected invention. Specifically, the Office asks:

> What is the purpose or objective of practicing the invention? Why would the artisan use the invention to detect a PCGEMI nucleic acid molecule in a biological sample? How is the scientific data or information procured by the practice of the invention necessarily used, if at all? If not a mere step in the disclosed process of detecting

> (diagnosing) prostate cancer, how else might Applicant intend the process, that is now claimed, be used?

Office Action at 22. As discussed above in response to the 35 U.S.C. §101 rejection, the specification discloses several utilities for the claimed methods of detecting a PCGEM1 nucleic acid in a biological sample. Thus, in response to the above inquiries, one of skill in the art would understand from the specification that the claimed methods could be used for more than simply detecting prostate cancer, including, for example, identifying an androgen-responsive cell line, measuring responsiveness to hormone-ablation therapy, and for analyzing abnormalities associated with diseases, such as diabetes mellitus, T cell leukemia and T cell lymphoma, that map to chromosome 2 and in particular to region 2q32.

The Office also asserts that "[t]o satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, the claims must define the metes and bounds of the subject matter that is regarded as the invention by Applicant with the clarity and particularity necessary to permit the skilled artisan to know or determine infringing subject matter." Office Action at 22. The Office then notes that "Applicant has argued that the claims are directed to a method of detecting a marker for diseases associated with the 2q32 region of chromosome 2." *Id.*; *see also* Applicant Response dated 7 December 2007 at 15 (stating that the "claims are directed to a method of detecting a marker for diseases associated with the 2q32 region of chromosome 2."). In response to this statement, the Office asserts that "the claims are not directed to such subject matter; rather the claims are directed to a process for detecting a PCGEM1 nucleic acid in a biological sample comprising intact cells." Office Action at 22.

This statement from Applicant's previously filed response requires clarification. According to the plain language, claims 22-30 are directed to a method of detecting a PCGEM1 nucleic acid in a biological sample comprising:

combining the biological sample with a nucleic acid comprising at least 10 contiguous nucleotides of SEQ ID NO:1 under hybridizing conditions; and

detecting hybridization between the nucleic acid comprising at least 10 contiguous nucleotides of SEQ ID NO:1 and the PCGEM1 nucleic acid in the biological sample, wherein hybridization indicates the presence of the PCGEM1 nucleic acid in the biological sample.

Applicant submits that there is nothing vague or ambiguous about the language of the claims. If the Office continues to maintain this rejection, Applicant requests that the Office identify the term or terms that allegedly renders the metes and bounds of the claimed subject matter uncertain. Any method of detecting a PCGEM1 nucleic acid that includes combining a biological sample with the recited nucleic acid under hybridizing conditions and detecting hybridization is covered by the claims. Thus, as discussed in the specification, detecting a PCGEM1 nucleic acid in a biological sample can be used, for example, to analyze abnormalities associated with gene mapping to chromosome 2 and in particular to region 2q32, which is known to be associated with specific diseases, including diabetes mellitus and T cell leukemia/lymphoma. As known in the art, chromosomal abnormalities can be detected using various techniques, including *in situ* hybridization, which usually involves treating sample cells or tissues to fix the target transcripts in place, combining the sample with a nucleic acid probe under hybridizing conditions and detecting hybridization. Accordingly, the claimed methods recite the clarity and particularity necessary to permit the skilled artisan to know or determine infringing subject matter, and Applicant requests that the Office withdraw this rejection.

The Office also maintains an additional rejection of claims 22-30 under 35 U.S.C. §112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter the applicant regards as the invention." Office Action at 23. Specifically, the Office asserts that the phrase "under hybridizing conditions" is vague and indefinite and "does

not provide a standard for ascertaining the requisite degree of stringency that must be used in practicing the claimed invention." Office Action at 23-24.

Although Applicant disagrees, in an effort to expedite prosecution, claim 22 has been amended to recite hybridizing conditions of "moderate stringency." As discussed in the specification, a person of ordinary skill in the art can readily determine conditions of moderate stringency. Specification at page 9, line 24 to page 10, line 6. The specification also cites a standard manual, Sambrook et al., that sets forth the basic conditions of moderate stringency and explains that the skilled artisan will know how to adjust conditions, such as temperate, wash solution, and salt concentration as necessary according to factors such as the length of the hybridization probe. *Id.* Accordingly, Applicant respectfully requests that the Office withdraw this 35 U.S.C. §112, second paragraph rejection.

VII. Rejections Under 35 U.S.C. §112, First Paragraph

A. Enablement

The Office maintains its rejection of claims 22-30 under 35 U.S.C. § 112, first paragraph, asserting that "the claimed invention is not supported by either a specific and substantial utility or a well-established utility for the reasons set forth above" and therefore concludes that "one skilled in the art clearly would not know how to use the claimed invention." Office Action at 25. Applicants respectfully traverse this rejection.

As discussed above in response to the 35 U.S.C. § 101 rejection, the specification discloses several specific and substantial utilities for the claimed method of detecting a PCGEM1 nucleic acid in a biological sample. As such the methods of claims 22-30 are not a mere "invitation to elaborate or develop a useful process comprising the active step of detecting a PCGEM1 nucleic acid in a biological sample." *See* Office Action at 25.

Under the Utility Examination Guidelines, when an Applicant satisfactorily rebuts a *prima facie* rejection based on lack of utility under 35 U.S.C. 101, the Office must not only withdraw the 101 rejection but must also withdraw the corresponding rejection under 35 U.S.C. § 112, first paragraph. (Utility Examination Guidelines, 66 Fed. Reg. 1092, 1099 (2001).) In view of the arguments presented above, with respect to the utility of the claimed invention, the Applicant respectfully requests the Office to withdraw its enablement rejection under 35 U.S.C. § 112, first paragraph.

2. Written Description

The Office maintains the rejection of claims 22-30 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that is not described in the specification so as to reasonably convey to the person skilled in the art that Applicant was in possession of the claimed invention at the time the application was filed. Office Action at 26-27. Applicant respectfully traverses this rejection.

As an initial matter, the Office argues that the claims do not comply with the written description requirement "[b]ecause the claimed invention has no objective or purpose, apart from the acquisition of scientific data or information concerning the presence of a PCGEMI nucleic acid molecule, it is not possible to practice the claimed invention to achieve any one particular effect." *Id.* at 28. As discussed above, the specification discloses several specific and substantial utilities for the methods of claims 22-30, thus rendering this aspect of the Office's written description rejection moot.

The Office also argues that the members of the genus of PCGEM1 nucleic acids may vary substantially and that the specification fails to describe members of the genus as sharing a distinguishing identifying characteristic. *Id.* at 29-31. Applicant notes that the claimed methods are not directed to a PCGEM1 nucleic acid. Nor are they directed to a method of using a PCGEM1

nucleic acid. Rather they are directed to a method of detecting a PCGEM1 nucleic acid using a nucleic acid comprising at least 10 contiguous nucleotides of SEQ ID NO:1. As such, Applicant does not need to show possession of a genus of PCGEM1 nucleic acids that can be detected using the claimed method. Rather, Applicant has disclosed a unique nucleic acid probe having at least 10 (claim 22) or 17 (claim 27) contiguous nucleotides of SEQ ID NO:1 that can be used under stringent conditions to detect structurally similar PCGEM1 nucleic acids. In view of the pending claims under examination, Applicant needs to show possession of a method of detecting a PCGEM1 sequence using a nucleic acid comprising at least 10 contiguous nucleotides of SEQ ID NO:1, and have done so.

In support of this written description rejection, the Office relies on *University of Rochester v. G.D. Searle* Co., 358 F.3d 916, 922, 69 USPQ2d 1886, 1892 (Fed. Cir. 2004) for the proposition that "[r]egardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods." However, the facts of the present application are distinguishable from those in *University of Rochester*.

Scientists at the University of Rochester had discovered a second COX enzyme, COX-2, and postulated that a non-steroidal compound that specifically inhibited COX-2 without affecting COX-1, might possess the desirable anti-inflammatory properties of traditional NSAIDS while avoiding the undesirable gastrointestinal side effects associated with traditional COX-1 inhibitors. But the patent application did not disclose a single compound that could be used to specifically inhibit COX-2. Nor did it provide any guidance as to what types of molecules might posses such properties. Nevertheless, the University of Rochester obtained a patent with claims directed to methods of treating a patient with a non-steroidal COX-2 inhibitor. The Federal

Circuit held that those claims were invalid for failing to satisfy the written description requirement, noting that the "patent does not provide any guidance that would steer the skilled practitioner toward compounds that can be used to carry out the claimed methods — an essential element of every claim of that patent." *Id.* Thus, in *University of Rochester*, the claims were directed to methods of *using a compound* that was defined solely in functional terms. The instant claims, on the other hand, are not directed to a method of using a PCGEM1 nucleic acid, but rather to a method of detecting such a nucleic acid. The skilled practitioner does not need to know the sequence of a specific PCGEM1 nucleic acid to practice the claimed method. Instead, by carrying out the steps of the method using a sequence having at least 10 contiguous nucleotides of SEQ ID NO:1 under stringent conditions, one of skill in the art can detect whether or not a PCGEM1 nucleic acid is present in a sample. As such, the claimed methods are distinguishable from the methods at issue in *University of Rochester*.

Moreover, even if required to show possession of a genus of PCGEM1 nucleic acids that could be obtained by the claimed method, Applicant submits that the instant specification satisfies this requirement.

In *Enzo Biochem., Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 U.S.P.Q.2d 1609 (Fed. Cir. 2002), the Court of Appeals for the Federal Circuit addressed the compliance of genus claims to nucleic acids based on their hybridization properties with the written description requirement of 35 U.S.C. § 112, first paragraph. Enzo's claims were directed to nucleic acids that selectively hybridized to a particular species of bacteria. 296 F.3d at 1321-22, 63 U.S.P.Q.2d at 1611. The court provided guidance as to how to determine whether genus claims to nucleic acids based on their hybridization properties fulfill the written description requirement of 35 U.S.C. § 112, first paragraph:

> The PTO has also provided a contrasting example of genus claims to nucleic acids based on their hybridization properties, and has determined that such claims may be adequately described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar. *See id.*, Example 9, at 35-37. Whether the disclosure provided by the three deposits in this case, coupled with the skill of the art, describes the genera of claims 1-3 and 5 is a fact question the district court did not address. On remand, the district court should determine, consistently with the precedent of this court and the PTO's Guidelines, whether one skilled in the art would consider the subject matter of claims 1-3 and 5 to be adequately described, recognizing the significance of the deposits and the scope of the claims.

296 F.3d at 1327-28, 63 U.S.P.Q.2d at 1615.

Thus, in *Enzo*, the Federal Circuit cited the PTO's Guidelines with respect to compliance of genus claims to nucleic acids based on their hybridization properties with the written description requirement of 35 U.S.C. § 112, first paragraph. This type of claim may be adequately described because the hybridization conditions may dictate that all species within the genus will be structurally similar.

Application of the analysis set forth in *Enzo* demonstrates that Applicant's claims 22-30 are adequately described because the recitations in Applicant's claims dictate that all PCGEM1 nucleic acids that can be detected by the claimed method will be structurally similar. Similar to the hybridization language in the claims at issue in *Enzo*, claim 22 recites a step of combining a nucleic acid comprising at least 10 contiguous nucleic acids of SEQ ID NO:1 with a biological sample under stringent conditions. As in *Enzo*, this recitation in the claims imposes a structural limitation on any PCGEM1 nucleic acid detectable by the claimed method and dictates that all such PCGEM1 nucleic acids will be structurally similar to the nucleic acid comprising at least 10 contiguous nucleotides of SEQ ID NO:1. Thus, according to the test set forth in *Enzo*, Applicant's claims 22-30 fulfill the requirements of 35 U.S.C § 112, first paragraph.

For these reasons, Applicant requests that the Office reconsider and withdraw this written description rejection.

The Office also rejects claims 22-30 under 35 U.S.C. § 112, first paragraph alleging that the phrase "comprising intact cells" represents new matter. Office Action at 36-39. In an effort to more clearly delineate the scope of the claimed subject matter and avoid any confusion, Applicant proposes to amend claim 22 by removing the word "intact."

As noted by the Office, one of skill in the art would appreciate, particularly in view of claim 23, that the steps of the claimed method need not be carried out on intact cells and that the process could comprise a step of isolating the nucleic acid from the cells in the biological sample. Applicant agrees. Furthermore, there is ample support in the specification for detecting a PCGEM1 nucleic acid in a biological sample comprising cells, where the nucleic acid is isolated from the cells or otherwise made accessible prior to detecting hybridization, including, for example:

- Example 2 ("The full length of PCGEM1 was obtained by 5' and 3' RACE/PCR from the original 530 bp DD product (nucleotides 410 to 940 of PCGEM1 cDNA SEQ ID NO:1 using a normal prostate cDNA library . . . . We also used the original DD product to screen a normal prostate cDNA library. Three overlapping cDNA clones were identified.")
- Example 3 ("PCGEM1-Bac clone 1 DNA was nick translated using spectrum orange (Vysis) as a direct label and fluorescent *in situ* hybridization was done using this probe on normal human male metaphase chromosome spreads.")
- Example 4 ("DNA-free RNA was prepared from these tissues and used in RT-PCR analysis to detect PCGEM1 expression.")

- Example 5 ("Paired normal (benign) and tumor specimens from 13 patients were tested using *in situ* hybridization. A representative example is shown in FIG. 17. In 11 cases (84%) tumor associated elevation of PCGEM1 expression was detected.")
- Example 6 ("To test if PCGEM1 expression is regulated by androgens, we performed experiments evaluating PCGEM1 expression in LNCaP cells (ATCC) cultured with and without androgens. . . . Poly A+ RNA derived from cells treated with/without R1881 was extracted at indicated time points with RNAzol B (Tel-Test, Inc, TX) and fractionated (2 μg/lane) by running on 1% formaldehyde-agarose gel and transferred to nylon membrane. Northern blots were analyzed for the expression of PCGEM1 using the nucleic acid molecule set forth in SEQ ID NO: 4 as a probe. The RNA from LNCaP cells treated with R1881 and RNA from control LNCaP cells were also analyzed by RT-PCR assays as described in Example 4.")
- Example 7 ("Polyadenylate RNAs of 23 different human tissues (heart, brain, placenta, lung, liver skeletal muscle, kidney, pancreas, spleen, thymus, prostate, testis, ovary, small intestine, colon, peripheral blood, stomach, thyroid, spinal cord, lymph node, trachea, adrenal gland and bone marrow) were probed with the 530 base pair PCGEM1 cDNA fragment (nucleotides 410 to 940 of SEQ ID NO:1). A 1.7 kilobase mRNA transcript hybridized to the PCGEM1 probe in prostate tissue (FIG. 6a).")

Given the support in the specification, Applicant respectfully requests the Office to withdraw this new matter rejection.

VIII. Rejections Under 35 U.S.C. § 102

1. Srikantan

The Office rejects claims 22-25 and 27-30 under 35 U.S.C. §102(b) as allegedly anticipated by Srikantan et al. (*Srikantan*). Office Action at 32. An invention properly asserted as anticipatory under 35 U.S.C. § 102(b) must have been published more than one year prior to the Applicant's effective filing date. For the reasons of record, Applicant's priority claim reaches back to the date of the related provisional application, and thus the effective filing date is March 26, 1999. *Srikantan* was published after the Applicant's effective filing date thus does not qualify as 35 U.S.C. §102(b) art. The Office is thus respectfully requested to withdraw this rejection.

2. Dixon in View of Srikantan

The Office rejects claims 22-25 and 27-30 under 35 U.S.C. §102(b) as allegedly anticipated by Dixon et al. (*Dixon*) in view of *Srikantan*. Office Action at 33. As set forth above, a reference which anticipates the invention under 35 U.S.C. § 102(b) must have been published more than one year prior to the Applicant's effective filing date. *Dixon*, like *Srikantan* was published after the Applicant's effective filing date thus does not qualify as 35 U.S.C. §102(b) art. Applicant thus respectfully requests the Office to withdraw the rejection under 35 U.S.C. § 102(b) as anticipated by *Dixon*, as evidenced by *Srikantan*.

IX. Obviousness-Type Double Patenting Rejections

The Office maintains the rejection of claims 22, 23, and 27-29 under nonstatutory obviousness-type double patenting in view of claims 1-9 of U.S. Patent No. 6,828,429. Office Action at 35. Applicants will consider submitting a terminal disclaimer, if appropriate, when the

pending claims in the present application are indicated as allowable. The filing of a terminal disclaimer to obviate a rejection based on nonstatutory double patenting is not an admission of the propriety of the rejection. *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20 USPQ2d 1392 (Fed. Cir. 1991).

X. Conclusion

Applicant believes that all of the substantive issues raised in the Final Office Action mailed 4 March 2008 have been addressed, and all objections and rejections overcome. Accordingly, Applicant believes that this application is in condition for allowance. If the Office believes anything further is required in order to place this application in even better condition for allowance, Applicant requests that their undersigned representative be contacted at the number listed below to discuss remaining issues.

Please grant any extensions of time required to enter this paper and charge any additional required fees to Deposit Account No. 50-3740.

Respectfully submitted,
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